Streptococcus pneumoniae (Invasive Disease)

Section 1: ABOUT THE DISEASE

A. Etiologic Agent

Invasive pneumococcal disease is caused by the bacterial pathogen *Streptococcus pneumoniae* (the pneumococcus). Pneumococci are lancet-shaped, gram-positive diplococci. Of the 90 capsular serotypes that have been identified, 23 serotypes are responsible for most invasive disease in the U.S. Serotypes 4, 6B, 9V, 18C, 19F, and 23F cause most invasive childhood pneumococcal infections in the U.S. Some of these and other serotypes cause most disease in adults. Increasing antibiotic resistance in this organism is an important public health problem.

B. Clinical Description

The pneumococcus is the most common cause of bacterial pneumonia and bacterial meningitis in the U.S. It is also the most common cause of acute otitis media and invasive bacterial infections in children. The pneumococci are a common cause of sinusitis and conjunctivitis in children. The pneumococci occasionally cause endocarditis, osteomyelitis, pericarditis, pyogenic arthritis, soft tissue infection, and early-onset neonatal septicemia. The pneumococci cause an estimated 3,000 cases of meningitis; 63,000 cases of bacteremia; 125,000 hospitalizations due to pneumonia; and 6,800,000 cases of acute otitis media each year. Approximately 10% of all patients with invasive pneumococcal disease die of their illness, but case-fatality rates for the elderly and patients with underlying illnesses can exceed 50%, even with antimicrobial therapy.

C. Vectors and Reservoirs

Humans are the only known reservoir. Pneumococci are commonly found in the upper respiratory tract of healthy people worldwide.

D. Modes of Transmission

Pneumococci can be spread from person to person by respiratory droplets. While person-to-person transmission of the organisms is common, illness among casual contacts and attendants is rare. Invasive disease arises in colonized individuals related mostly to host factors.

E. Incubation Period

The incubation period varies by type of infection, and it is difficult to establish because most people acquire the organism as colonization of the airway and disease does not result.

F. Period of Communicability or Infectious Period

The infectious period is generally unknown. Because organisms are transmitted but disease does not usually result, isolation of colonized or infected people is not necessary.

G. Epidemiology

Pneumococci are ubiquitous, with many healthy people having colonization in their upper respiratory tracts. The pneumococcal serotypes most often responsible for causing infection are those most frequently found in carriers. The spread of the organism within a family or household is influenced by such factors as crowding, season, and the presence of viral upper respiratory infections, including influenza. The incidence of pneumococcal disease is usually associated with increased carriage rates, but high carriage rates do not necessarily increase the risk of disease in households. Pneumococcal infections are most prevalent during winter months; are most common in infants, young children, and the elderly; and are more common in African-American and some American Indian populations than in other racial and ethnic groups. An increased risk of invasive pneumococcal disease has been associated with daycare attendance.

Outbreaks of pneumococcal pneumonia are rare. When outbreaks occur, they are usually in crowded environments, such as jails and nursing homes.

Pneumococcal infections are of increased incidence and severity in people who are immunocompromised due to HIV infection, have functional or anatomical asplenia (especially sickle cell disease), have chronic heart or lung disease, or have other chronic medical conditions.

H. Bioterrorist Potential

This pathogen is not considered to be of risk for use in bioterrorism.

Section 2:
REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

- *S. pneumoniae*, invasive disease, should be reported to the local board of health (LBOH) in the community where the case is diagnosed or suspect case is identified.
- Isolation of *S. pneumoniae* from a usually sterile site should be reported directly to the MDPH within 24 hours.
- All cases of invasive antibiotic-resistant *S. pneumoniae* should be reported to the MDPH.

B. Laboratory Testing Services Available

Definitive diagnosis of pneumococcal infection is by the recovery of *S. pneumoniae* from a normally sterile body site (e.g., blood, cerebrospinal fluid [CSF], pleural fluid, or peritoneal fluid).

Because pneumococci frequently colonize the upper respiratory tract in the absence of the disease, the clinical significance of recovering the organism from non-sterile sites (e.g., expectorated sputum, conjunctiva) is less certain.

Gram stain may be helpful in interpreting cultures of expectorated sputum; finding a predominance of gram-positive diplococci of typical morphology and >25 leukocytes with <10 epithelial cells per high power field on a microscopic examination of sputum supports the diagnosis of pneumococcal pneumonia. Positive blood or pleural fluid cultures confirm diagnosis.

Based on recommendations of the Clinical and Laboratory Standards Institute, clinical laboratories should test all isolates of *S. pneumoniae* from CSF for resistance to penicillin, cefotaxime or ceftriaxone, meropenem, and vancomycin. For organisms from other sources, laboratories should consider testing for resistance to erythromycin, penicillin, trimethoprim-sulfamethoxazole, clindamycin, cefepime, cefotaxime or ceftriaxone, a fluoroquinolone, meropenem, tetracycline, and vancomycin. Pneumococci resistant to vancomycin have not been described; a strain with a minimum inhibitory concentration of ≥2 µg/ml of vancomycin or zone diameter of <17mm in a standard disk diffusion susceptibility test using a 30 µg vancomycin disk should be submitted to a reference laboratory for confirmatory testing, and if resistant, should be reported to the MDPH.

Clinical laboratories should submit *S. pneumoniae* isolates from sterile sites, along with the antimicrobial susceptibility testing results, to the MDPH State Laboratory Institute (SLI) using the SLI *Specimen Submission Form* found at the end of this chapter and on the MDPH website at www.mass.gov/dph/bls/generalform.pdf.

Serotyping is performed in a very limited number of laboratories. The Centers for Disease Control and Prevention (CDC), Streptococcal Reference Laboratory serotypes pneumococcal isolates from blood, CSF, or other sterile sites from episodes of bacteremia or meningitis occurring in children who have received pneumococcal conjugate vaccine as part of an effort to monitor the effect of the pneumococcal conjugate vaccine. The SLI forwards selected specimens to the CDC for serotyping.

For more information on submitting specimens, contact the SLI Reference Laboratory at (617) 983-6607. Remember, when submitting any clinical specimens to the SLI, you must use the SLI *Specimen Submission Form* found at the end of this chapter and on the MDPH website at www.mass.gov/dph/bls/generalform.pdf.

In certain outbreak investigations conducted by MDPH staff, the SLI Reference Laboratory will test clinical specimens for the presence of *S. pneumoniae* and send isolates to the CDC for serotyping.

Section 3:
REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To define national and local trends in pneumococcal disease.
- To monitor the impact of the use of pneumococcal polysaccharide vaccine (PPV23) and pneumococcal conjugate vaccine, 7-valent (PCV7) on disease.
- To detect geographic and temporal changes in the prevalence of antimicrobial drug-resistant *S. pneumoniae.*

B. Laboratory and Health Care Provider Reporting Requirements

S. pneumoniae, invasive infection, is reportable to the LBOH. The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of *S. pneumoniae* invasive disease and invasive antibiotic-resistant *S. pneumoniae*, as defined by the reporting criteria in Section 2A.

Any cluster of invasive pneumococcal disease should be reported immediately to the LBOH and to the MDPH at (617) 983-6800 or (888) 658-2850.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of *S. pneumoniae* from a normally sterile site and antibiotic-resistant *S. pneumoniae* from any site shall report such evidence of infection directly to the MDPH within 24 hours.

C. Local Board of Health (LBOH) Reporting and Follow-up Responsibilities

Reporting Requirements

MDPH regulations *(105 CMR 300.000)* stipulate that invasive pneumococcal disease is reportable to the LBOH and that each LBOH must report any case of invasive pneumococcal disease or suspect case of invasive pneumococcal disease, as defined by the reporting criteria in Section 2A. Cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using a MDPH *Invasive Streptococcus Pneumoniae Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

Case Investigation for Individuals <18 Years of Age

1. Ensure that the specimen has been sent to the SLI for serotyping. Call an epidemiologist at the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, for assistance.
2. Collect pertinent information from the health care provider, including demographic, clinical, detailed pneumococcal immunization history (e.g., PCV7 and PPV23, and other vaccine given the same day as the last dose of pneumococcal vaccine), as well as other pertinent history on the case, and record the information on the MDPH *Invasive Streptococcus Pneumoniae Case Report Form*.
3. Contact the family to complete the family history portion on the case report form, and inquire about childcare attendance or institutional settings.
4. Assess vaccination status of the case and contacts.
5. Determine if the case has indications for pneumococcal vaccine, and recommend age-appropriate vaccination with either PCV7 or PPV23.
6. If the child attends childcare or an institutional setting, the facility should be contacted to inform them of the case. Use the case as an educational opportunity. The director should review children's vaccination records and the records of anyone identified to be at high risk of pneumococcal disease to verify that those individuals are up to date for PCV7 (or PPV23, if appropriate). Parents of those children not up to date should be reminded to have their children age-appropriately immunized.
7. If the case is less than five years old and has received at least one dose of PCV7, it is very important to collect the following information:

a. Contact the provider and ask whether the patient has been evaluated for an immune disorder, has had his/her spleen or splenic function evaluated, or has had any other testing to evaluate immunologic function.

b. Be sure to obtain a complete pneumococcal immunization history (e.g., PCV7 and PPV23, and other vaccine given the same day as the last dose of pneumococcal vaccine).

c. Ask if a *Vaccine Adverse Events Reporting System (VAERS) Form* was completed. If not, recommend that it be done now. VAERS forms can either be downloaded or can be completed electronically at the VAERS website at www.vaers.hhs.gov.

d. If you have made several attempts to obtain case information but have been unsuccessful (e.g., the case or health care provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as you have gathered. Please note on the form the reason(s) why it could not be filled out completely.

Case Investigation for Individuals ≥18 Years of Age

1. It is the responsibility of the LBOH to complete a MDPH *Invasive Streptoccocus Pneumoniae Case Report Form* (found at the end of this chapter).
2. Use the following guidelines to assist in completing the form:
   a. Accurately record the demographic information.
   b. Accurately record clinical information, including the date of symptom onset, symptoms, whether hospitalized, type of infection(s), and hospital and clinician contact information.
   c. Indicate whether the patient had any significant underlying illness(es).
   d. Indicate the specimen(s) from which *S. pneumoniae* was isolated, and what type of laboratory tests were performed. If susceptibility testing was performed, please attach the results.
   e. Determine whether the patient resides in a long-term care facility; indicate which facility and record whether the patient was vaccinated with PPV23.
   f. If the case is 18 years of age or older, stop here. Do not complete page 3 of the MDPH *Invasive Streptoccocus Pneumoniae Case Report Form*.
   g. If you have made several attempts to obtain case information but have been unsuccessful (e.g., the case or health care provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as you have gathered. Please note on the form the reason(s) why it could not be filled out completely.
3. After completing the case report form, attach laboratory report(s) and fax or mail (in an envelope marked "Confidential") to ISIS. The confidential fax number is (617) 983-6813. Call ISIS at (617) 983-6801 to confirm receipt of your fax. The mailing address is:

MDPH, Office of Integrated Surveillance and Informatics Services (ISIS)
305 South Street, 5th Floor
Jamaica Plain, MA 02130
Fax: (617) 983-6813

4. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.

Section 4: CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements *(105 CMR 300.200)*

Quarantine is not applicable. There are currently no isolation and quarantine regulations pertaining to invasive pneumococcal disease.

B. Protection of Contacts of a Case

1. There are no routine control measures other than recommended age-appropriate immunization.
2. PCV7 and PPV23 protect against 90% of invasive disease. Vaccination also decreases the need for antibiotics, therefore preventing antibiotic resistance. Investigation provides an opportunity to identify contacts with indications for pneumococcal vaccine.
3. PCV7 is recommended for:
   a. Routine immunization of all children 2–23 months of age;
   b. Children 24–59 months of age with the following high-risk medical conditions:
      i. Sickle cell disease;
      ii. Functional or anatomic asplenia;
      iii. HIV infection;
      iv. Immunosuppression caused by illness, treatment or medication; and
      v. Certain chronic medical diseases (e.g., cardiopulmonary disease, cochlear implants, CSF fluid leaks, renal failure, nephrotic syndrome, diabetes, liver disease).
4. PCV7 should be considered for all children 24–59 months of age, with prioritization given to:
   a. All children 24–35 months of age;
   b. All children 36–59 months of age who are African American, Alaskan Native or Native American; and
   c. All children attending out-of-home childcare ($\geq$4 hours per week with $\geq$2 unrelated children).

5. PPV23 is indicated for the following individuals:*

Immunocompetent Persons	Immunocompromised Persons*
◆ All persons 65 years of age and older ◆ Persons 2–64 years of age with: – Cardiovascular disease – Pulmonary disease (excluding asthma) – Diabetes – Alcoholism or chronic liver disease – CSF leaks – Sickle cell disease – Cochlear implants	Persons 2–64 years of age with: ◆ Functional or anatomic asplenia ◆ Leukemia, lymphoma, Hodgkin's disease, multiple myeloma, generalized malignancy ◆ Chronic renal failure or nephrotic syndrome ◆ Conditions, such as organ transplants, associated with immunosuppression – HIV infection – Immunosuppressive therapy, including long-term corticosteroids (equivalent to ≥2 mg/kg/day, or a total of ≥20 mg/day of prednisone, for ≥14 days) and radiation
Persons 2–64 years of age: ◆ Living in long-term care facilities ◆ Who are Native American	

* Including children who received PCV7, as long as it has been ≥2 months since the last dose of PCV7.

Please visit the MDPH web site at www.mass.gov/dph for the most up-to-date recommendations regarding the use of pneumococcal vaccine for children and adults, including recommendations for revaccination.

C. Managing Special Situations

Hospital Settings

Standard precautions are recommended.

Childcare Settings

Review the vaccination status of all children to ensure that their PCV7 status is up to date.

Other Institutional Settings

Follow standard precautions. Review the vaccination status of all residents. Immediately report any clusters to the LBOH and to the MDPH at (617) 983-6800 or (888) 658-2850.

D. Preventive Measures

Administer age-appropriate pneumococcal vaccine as outlined above. Please visit the MDPH web site at www.mass.gov/dph for the most up-to-date recommendations regarding the use of pneumococcal vaccine for children and adults.

ADDITIONAL INFORMATION

The following are the formal CDC surveillance case definitions for drug resistant *S. pneumoniae* (DRSP) invasive disease and invasive *S. pneumoniae.* They are provided for your information only and should not affect the investigation and reporting of a case that fulfills the criteria in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2A.

Note: The most up-to-date CDC case definitions are available on the CDC website at www.cdc.gov/epo/dphsi/casedef/case_definitions.htm.

Case Definition of Drug Resistant *S. pneumoniae* (DRSP) Invasive Disease

Clinical Description

S. pneumoniae causes many clinical syndromes, depending on the site(s) of infection (e.g., acute otitis media, pneumonia, bacteremia, or meningitis).

Laboratory Criteria for Diagnosis

Isolation of *S. pneumoniae* from a normally sterile site (e.g., blood, CSF, or less commonly, joint, pleural, or pericardial fluid).

A normally sterile site is defined as a portion of the human body in which no microorganisms are found in a healthy state and include the following: blood, CSF, pleural fluid, peritoneal fluid, pericardial fluid, bone, joint fluid, internal body site (lymph node, brain, heart, liver, spleen, vitreous fluid, kidney, pancreas, or ovary), or other normally sterile site.

Case Classification

Probable	A clinically compatible case caused by laboratory-confirmed culture of *S. pneumoniae* identified as "non-susceptible" (i.e., and oxacillin zone size of <20mm) when oxacillin screening is the only method of antimicrobial susceptibility testing performed.
Confirmed	A clinically compatible case caused by laboratory-confirmed culture of *S. pneumoniae* identified as "non-susceptible" according to the laboratory criteria listed above.

Case Definition of Invasive *S. pneumoniae*

Clinical Description

S. pneumoniae causes many clinical symptoms, depending on the site of infection (e.g., pneumonia, bacteremia, or meningitis).

Laboratory Criteria for Diagnosis

Isolation of *S. pneumoniae* from a normally sterile site (e.g., blood, CSF, or less commonly, joint, pleural, or pericardial fluid).

Case Classification

Confirmed	A clinically compatible case caused by laboratory-confirmed culture of *S. pneumoniae* from a normally sterile site.

Vaccine Information Statements (VIS) for all vaccines, including pneumococcal vaccine, inactivated and live, attenuated influenza vaccine are available in English and in many other languages at the Immunization Coalition website at www.immunize.org/vis.

REFERENCES

American Academy of Pediatrics. [Pneumococcal Infections.] In: Pickering L.K., ed. *Red Book: 2003 Report of the Committee on Infectious Diseases, 26th Edition*. Elk Grove Village, IL, American Academy of Pediatrics; 2003: 490–500.

Centers for Disease Control and Prevention (CDC). *Epidemiology and Prevention of Vaccine-Preventable Diseases, 8th Edition*. Atkinson, W., Hamborsky, J., Wolfe, S., eds. Washington DC, Public Health Foundation, 2004: 233–245.

CDC. *Manual for the Surveillance of Vaccine-Preventable Diseases*. CDC. Atlanta, GA 1999: 9.1–9.14.

CDC. Prevention of Pneumococcal Disease—Recommendations of the ACIP. *MMWR*. 1997; 46. <www.cdc.gov/mmwr/preview/mmwrhtml/00047135.htm>.

CDC. Preventing Pneumococcal Disease among Infants and Young Children—Recommendations of the ACIP. *MMWR*. 2000; 49. <www.cdc.gov/mmwr/preview/mmwrhtml/rr4909a1.htm>.

Heymann D., ed. *Control of Communicable Disease, 18th Edition*. Washington DC, American Public Health Association, 2004: 413–417.

MDPH. *Regulation 105 CMR 300.000: Reportable Diseases, Surveillance, and Isolation and Quarantine Requirements*. MDPH, Promulgated November 4, 2005.

FORMS & WORKSHEETS

Streptococcus pneumoniae

(Invasive Disease)

Streptococcus pneumoniae (Invasive Disease)

LBOH Action Steps

This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to invasive S. pneumoniae case investigation activities.

LBOH staff should follow these steps when invasive *S. pneumoniae* is suspected or confirmed in the community. For more detailed information, including disease epidemiology, reporting, case investigation, and follow-up, refer to the preceding chapter.

Reporting

- ❑ Notify the MDPH Division of Epidemiology and Immunization, at (617) 983-6800 or (888) 658-2850, to report any confirmed case(s) of *S. pneumoniae*.

Case Investigation

- ❑ Work with MDPH to ensure that appropriate clinical specimens are collected and submitted to the SLI for confirmation.
- ❑ Fill out the MDPH case report form, including clinical information, vaccination history, and laboratory results.
- ❑ If the case is 18 years of age or older, page three of the case report form does not need to be completed.
- ❑ Send the completed case report form (with laboratory results) to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).

Prevention and Control

- ❑ There are currently no routine control measures for cases of invasive pneumococcal disease.
  - ❑ However, it is important to use this opportunity to ensure that the case and contacts are appropriately vaccinated against pneumococcal disease if indicated (e.g., those <5 years of age, with high-risk medical condition, ≥65 years of age, or who live in an institutional setting).